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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,205	04/09/2004	Hong Zhao	213.1152-CIP	3686

20311 7590 04/20/2006

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,205	ZHAO ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-26* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This restriction requirement supersedes the restriction requirement mailed on December 27, 2005 and differs from the original requirement by addition of a species election.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-19, 21 drawn to an oligonucleotide pro-drug having the formula shown in claim 1, classifiable in class 536, subclass 23.1. Election of this group requires a further election of a single nucleotide sequence and a species election as set forth below.

II. Claim 20, drawn to an oligonucleotide pro-drug having the formula shown in claim 20, classifiable in class 536, subclass 23.1.

III. Claim 22, drawn to a method of making a prodrug having the formula R_2-L_4-L_3-X_1, classifiable in class 536, subclass 25.3.

IV. Claims 23-26, drawn to a method of treating a mammal for an undisclosed reason comprising administering the compound of claim 1, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

1. Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are patentably distinct compounds. Invention I

is directed to an oligonucleotide pro-drug having the formula shown in claim 1 while invention II is directed to an oligonucleotide pro-drug having the formula shown in claim 20.

2. Furthermore, examining invention I together with invention II would impose a serious search burden. In the instant case, prior art searches of oligonucleotide pro-drugs having the structure shown in claim 1 are not coextensive with prior art searches of oligonucleotide pro-drugs having the structure shown in claim 20. Search of each of these inventions would require different key word searches of each compound using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions I and II together.

3. Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions. Invention I is directed to an oligonucleotide pro-drug having the formula shown in claim 1 while the function of invention III is directed to a method of making a different prodrug.

4. Furthermore, examining invention I together with invention III would impose a serious search burden. In the instant case, prior art searches of oligonucleotide pro-drugs having the structure shown in claim 1 are not coextensive with prior art searches of methods of making an oligonucleotide pro-drug. Search of each of these inventions would require different key word searches of each compound used and each distinct

method step using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions I and III together.

5. Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process could be performed with a materially different product. For example, mammals can be treated with antibodies and small molecules.

6. Furthermore, examining invention I together with invention IV would impose a serious search burden. In the instant case, prior art searches of oligonucleotide pro-drugs having the structure shown in claim 1 are not coextensive with prior art searches of methods of treating a mammal with the compound of claim 1. Search of each of these inventions would require different key word searches of each compound and each distinct method step using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions I and IV together.

7. Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions. Invention II is directed to an oligonucleotide pro-drug having the formula shown in claim 20 while the function of invention III is directed to a method of making a different prodrug.

8. Furthermore, examining invention II together with invention III would impose a serious search burden. In the instant case, prior art searches of oligonucleotide pro-drugs having the structure shown in claim 20 are not coextensive with prior art searches of methods of making an oligonucleotide pro-drug. Search of each of these inventions would require different key word searches of each compound used and each distinct method step using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions II and III together.

9. Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions. Invention II is directed to an oligonucleotide pro-drug having the formula shown in claim 20 while the function of invention IV is to treat a mammal using the prodrug of claim 1.

10. Furthermore, examining invention II together with invention IV would impose a serious search burden. In the instant case, prior art searches of oligonucleotide pro-drugs having the structure shown in claim 20 are not coextensive with prior art searches of methods of treating a mammal with the compound of claim 1. Search of each of these inventions would require different key word searches of each compound and each distinct method step using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions II and IV together.

11. Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions. Invention III is directed a method of making an oligonucleotide pro-drug while the function of invention IV is to treat a mammal using the prodrug of claim 1.

12. Furthermore, examining invention III together with invention IV would impose a serious search burden. In the instant case, prior art searches of methods of making an oligonucleotide pro-drug are not coextensive with prior art searches of methods of treating a mammal with the compound of claim 1. Search of each of these inventions would require different key word searches of each compound and each distinct method step using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature,

placing a serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of inventions III and IV together.

Restriction to a single nucleotide sequence

Claim 8 is subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1)share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claim 8 specifically claims SEQ ID NOS 1-4. It is noted that SEQ ID NOS: 1, 2 and 4 are closely related but these sequences are structurally and functionally independent and distinct from SEQ ID NO: 3 due to their unique nucleotide sequences. As such the Markush/genus of antisense sequences in claim 8 is not considered to

constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the sequences claimed in claim 8 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search in terms of computer time needed to perform the search and the subsequent analysis of the search results by the examiner. In view of the foregoing, one (1) sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) sequence from SEQ ID NO: 1 (and related sequences) and SEQ ID NO: 3. Note that this is not a species election.

Species Election

Claim 1 is generic to the following disclosed patentably distinct species: the structures disclosed as being L_4 and L_1 in claims 11 and 12. The species are independent or distinct because the structures shown in the claims have different core structures, for example the branched alkyl structure illustrated at the bottom of page 60 has a different core structure than those with aromatic ring structures. A search of this branched structure would not be coextensive with a search of the species comprising aromatic rings. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tracy Vivlemore
Examiner
Art Unit 1635

TV
April 13, 2006

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER